

Support for new claim 126 can be found throughout the specification, and at least at claim 1 as originally filed, and claim 14.

Support for new claim 127 can be found throughout the specification, and at least at claim 53 as originally filed, and claim 68.

Support for new claim 128 can be found throughout the specification, and at least at page 4, lines 30-35 and page 39, lines 22-37.

REMARKS

Claims 1, 4-23, 53, 56-63, 65-81, and 120-128 are pending. Claims 2, 3, 24-52, 54, 55, 64, and 82-119 were previously canceled. Claims 17, 77, and 121-123 have been amended. Claims 126-128 have been added. Claims 15, 23, 69, and 79 are allowable. Reconsideration of the pending claims is respectfully requested. The paragraph numbering follows that of the Office Action.

Rejections Under 35 U.S.C. §103

¶6. Claims 1, 4-6, 8, 11, 13, 14, 16-19, 21, 22, 53-58, 60, 63, 65-68, 70, 72-75, 77, 78, 80, and 120-122 were rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Lou et al., Clin. Chem. 39(4):619-24 (1993) ["Lou"] in view of Maggio et al., Edward T. Maggio, Ed., pp. 61, 184-5 (1987) [Maggio"]. This rejection is respectfully traversed.

Lack of Motivation To Combine the Cited References

To establish a *prima facie* case of obviousness, the Office must show that there is some suggestion or motivation, either in the references themselves or in the knowledge generally available to the artisan, to modify the reference or to combine references to arrive at the claimed invention. Further, there must be evidence suggesting the modification would be successful. Applicants respectfully submit such a showing has not been made.

Briefly, claim 1 is directed to a method of quantifying analyte in a sample by (1) providing a lateral flow matrix that includes a sample receiving zone, a labeling zone containing diffusively bound a labeled first sbp member complementary to the analyte, and one or more serially oriented capture zones containing an immobilized second sbp member complementary to the analyte, (2) contacting sample with the sample receiving zone, (3) observing a pattern of label at the capture zones, and (4) correlating the pattern to an amount of analyte in the sample.

In contrast, Lou reports a one step competitive assay for measuring Lp(a) in plasma, including the steps of (1) providing a test strip that includes a sample loading area, a conjugate pad containing Lp(a)-coated colloidal selenium, and a series of measurement regions containing immobilized Lp(a)-specific monoclonal antibody, (2) applying serum, plasma, or whole blood to the sample loading area, (3) observing the number of measurement regions seen, and (4) correlating the number of regions seen to a concentration of Lp(a) protein in the sample. Yet Lou fails to teach certain elements of the claimed invention. For instance, Lou does not disclose an assay that provides a labeling zone containing a labeled first sbp member complementary to the analyte.

Maggio discusses a conventional enzyme immunoassays in both the competitive and sandwich formats. The conventional sandwich format includes the steps of (1) reacting the analyte with immobilized antibody, (2) washing the matrix, (3) reacting the washed matrix with an enzyme-antibody conjugate, (4) washing the matrix again, and (5) quantitating the enzyme reaction.

The Examiner suggests it would have been obvious to the artisan to modify the one-step competitive assay of Lou with the conventional sandwich format enzyme immunoassay of Maggio to arrive at the presently claimed invention because Maggio teaches that sandwich assays have the advantage of obviating the need for an antigen reagent. Applicants respectfully submit, however, that this analysis ignores certain disadvantages of the sandwich enzyme immunoassay observed by Maggio. For instance, Maggio reports that the sandwich format requires an additional wash step. Thus, there is ambiguity regarding the motivation to combine the references.

What is more, Applicants submit there are important differences between Maggio and Lou that fail to make their combination obvious. First, the conventional assays discussed by Maggio are performed in single wells. These assays have no zones, and do not involve reagents flowing on a strip. Second, the conventional assays of Maggio involve multiple wash steps, in contrast to the one-step format of Lou. Applicants submit there is no teaching or suggestion in Maggio that would motivate the artisan to take the sandwich assay format from Maggio and apply it to the one-step test strip assay of Lou. Nor is there teaching in Lou motivating the artisan to take the sandwich assay format from Maggio and apply it to the one-step test strip assay of Lou.

It is well established that simply because references can be combined, does not mean the resulting combination is obvious, unless the references also suggest the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). Applicants respectfully submit that no such desirability of the combination is suggested by the references.

Thus, Applicants maintain that the cited references fail to teach or even remotely suggest that a sandwich format used in a conventional enzyme immunoassay should similarly be used in a lateral flow assay. The Office Action has not established a motivation to combine the one-step assay of Lou with the conventional enzyme immunoassay of Maggio to arrive at the presently claimed invention.

Cited References Fail To Provide Expectation of Success

Applicants respectfully submit that the Office Action has not provided evidence that the proposed modification of Lou by Maggio would successfully result in the claimed invention.

As noted above, while Lou discusses a one step competitive test strip assay, Maggio discusses conventional enzyme immunoassays that require wash steps. Yet each of the cited references fail to teach that sandwich enzyme immunoassays can be successfully adapted for use in a lateral flow format. Further, each fails to teach that sandwich enzyme immunoassays can be successfully adapted for use in a lateral flow format that quantifies an amount of analyte in a sample.

Additionally, Maggio is ambivalent about the advantages and disadvantages of competitive and sandwich enzyme immunoassays. At best, the combination of Lou (one-step competitive assay for quantifying analyte) with Maggio (conventional multi-step competitive and sandwich assays) may possibly provide the artisan with an invitation to vary the parameters by *trying* a lateral flow sandwich assay for quantifying analyte. But this also is insufficient; the combination does not provide the artisan with a reasonable expectation of success of arriving at the claimed invention.

What is more, Lou actually reports unexplained discrepancies between a conventional sandwich enzyme immunoassay (Terumo) and their competitive one-step assay. See Lou at page 622, right column, second to last paragraph. The Terumo sandwich assay is discussed further at page 621, left column, last paragraph. Consequently, it is respectfully submitted that Lou in fact casts further doubt that the artisan would reasonably expect the combination of the cited references to successfully result in the presently claimed invention. The cited references fail to demonstrate that the sandwich assay of Maggio can successfully be translated to the one-step quantitative assay of Lou.

Applicants also note that the combination of cited references has been known to the public since 1993. Yet to Applicants knowledge, at the time the present application was filed, there were no published reports of any lateral flow quantitative assay comparable to that developed and presently claimed. During the period between 1993 and 1997 substantial research related to lateral flow assays was carried out, and efficient methods for performing lateral flow quantitative assays would have been welcomed by the scientific and medical communities. Applicants submit that the absence of scientific literature of any report of the allegedly obvious method is a classical indicium unobviousness.

Relatedly, according to MPEP 2141.01 (III), the content of the cited references must be considered at the time the invention was made, to avoid hindsight. The Office must "occupy the mind of one skilled in the art who is presented with the references, and who is normally guided by the then-accepted wisdom in the art."

Applicants respectfully submit that at the time the invention was made, the artisan would not have found the presently claimed invention to be obvious in light of the cited references.

Based on the above, Applicants submit the Office Action has not shown a motivation to combine the cited references to arrive at a method of quantifying analyte in a sample by (1) providing a lateral flow matrix that includes a sample receiving zone, a labeling zone containing diffusively bound a labeled 1st sbp member complementary to the analyte, and one or more serially oriented capture zones containing an immobilized 2nd sbp member complementary to the analyte, (2) contacting sample with the sample receiving zone, (3) observing a pattern of label at the capture zones, and (4) correlating the pattern to an amount of analyte in the sample. Further, the Office Action has not shown that artisan, at the time the invention was made, would reasonably expect the combination of references to successfully result in such a method. Applicants respectfully submit, therefore, that *prima facie* obviousness has not been established. Withdrawal of this rejection is respectfully requested.

Claims 4-6, 8, 11, 13, and 14 depend from, and incorporate the elements of, claim 1. Applicants respectfully submit that since a *prima facie* case of obviousness has not been established for claim 1, it is requested that this rejection be withdrawn from these claims as well.

Claim 14 is directed to the quantitative sandwich assay of claim 1, further providing the step of observing a distance traversed by the label along a single capture zone. The assays of Lou and Maggio have been discussed above; each fail to disclose this claimed feature.

To establish a *prima facie* case of obviousness, the Examiner must show that the prior art reference, or references when combined, must teach or suggest all the claim limitations. Applicant respectfully submits this showing has not been made with respect to claim 14. Specifically, each of Lou and Maggio fail to teach an assay that includes the step of observing a distance traversed by a labeled first sbp member along a

single capture zone. Accordingly, withdrawal of this rejection as applied to claim 14 is respectfully requested.

Generally, claim 16 is directed to a method of quantifying analyte in a sample by (1) providing a lateral flow matrix that includes a sample receiving zone, a labeling zone containing diffusively bound a labeled first sbp member complementary to the analyte, and one or more serially oriented capture zones containing an immobilized second sbp member that is analogous to the analyte, (2) contacting sample with the sample receiving zone, (3) observing a pattern of label at the capture zones, and (4) correlating the pattern to an amount of analyte in the sample. The assays of Lou and Maggio have been discussed above; yet each fail to disclose a lateral flow assay providing a second sbp member that is analogous to the analyte.

Absent a showing that Lou or Maggio teach or suggest a lateral flow assay providing this claimed element, Applicants submit that a *prima facie* case of obviousness has not been established. Accordingly, withdrawal of this rejection as applied to claim 16 is respectfully requested.

Claims 17-19, 21, and 22 depend from, and incorporate the elements of, claim 16. Applicants respectfully submit that since a *prima facie* case of obviousness has not been established for claim 16, it is requested that this rejection be withdrawn from these claims as well.

Briefly, claim 53 is directed to an assay device corresponding to the method of claim 1. For many of the reasons given above with respect to claim 1, Applicants submit that the Office Action has not made a showing that claim 53 is *prima facie* obvious.

Claims 56-58, 60, 63, 65-68, 71, and 122 depend from, and incorporate the elements of, claim 53. Applicants respectfully submit that since a *prima facie* case of obviousness has not been established for claim 53, it is requested that this rejection be withdrawn from these claims as well.

Generally, claim 72 is directed to an assay device corresponding to the method of claim 16. For many of the reasons given above with respect to claim 16,

Applicants submit that the Office Action has not made a showing that claim 72 is *prima facie* obvious.

Claims 73-75, 77, 78, and 80 depend from, and incorporate the elements of, claim 72. Applicants respectfully submit that since a *prima facie* case of obviousness has not been established for claim 72, it is requested that this rejection be withdrawn from these claims as well.

Claim 120 is directed to an assay kit corresponding to the device of claim 53. Applicants respectfully submit that for many of the reasons cited above with respect to claim 53, a *prima facie* case of obviousness has not been established for claim 120. Withdrawal of this rejection is respectfully requested.

As amended, claim 121 is directed to an assay kit corresponding to the device of claim 72. For many of the reasons cited above with respect to claim 72, Applicants submit that a *prima facie* case of obviousness has not been established for claim 121. Withdrawal of this rejection is respectfully requested.

¶7. Claims 7, 20, 59, and 76 were rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Lou in view of Maggio as applied to claims 1, 4-6, 8, 11, 13, 14, 16-19, 21, 22, 53-58, 60, 63, 65-68, 70, 72-75, 77, 78, 80, and 120-122, and further in view of US 4,740,468 to Weng et al. ["Weng"]. This rejection is respectfully traversed.

In brief, claims 7, 20, 59, and 76 are directed to assays and devices having the same elements recited in claims 1, 16, 53, and 72, respectively, wherein the assay further provides a second sbp member that is attached to an immobilized particle. Lou and Maggio are described above. Weng discusses an assay having an sbp member attached to an immobilized particle. Applicants submit that because a *prima facie* case of obviousness based on Lou and Maggio has not been established with regard to base claims 1, 16, 53, and 72 (see ¶6), this rejection in view of Weng is similarly improper. Withdrawal of the rejection is respectfully requested.

¶8. Claims 71 and 81 were rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Lou in view of Maggio as applied to claims 1, 4-6, 8, 11, 13, 14,

16-19, 21, 22, 53-58, 60, 63, 65-68, 70, 72-75, 77, 78, 80, and 120-122, and further in view of US 5,559,041 to Kang et al. ["Kang"]. This rejection is respectfully traversed.

Claims 71 and 81 are directed to assay devices having the same elements recited in claims 70 and 80, respectively, wherein the device further provides a common sample receiving zone. Kang discusses an assay having a common sample receiving zone. Applicants submit that because a *prima facie* case of obviousness based on Lou and Maggio has not been established with regard to base claims 70 and 80 (see ¶6), this rejection in view of Kang is similarly improper. Withdrawal of the rejection is respectfully requested.

¶9. Claims 9 and 61 were rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Lou in view of Maggio as applied to claims 1, 4-6, 8, 11, 13, 14, 16-19, 21, 22, 53-58, 60, 63, 65-68, 70, 72-75, 77, 78, 80, and 120-122, and further in view of US 4,496,654 to Katz et al. ["Katz"]. This rejection is respectfully traversed.

Claims 9 and 61 are directed to assays having the same elements recited in claims 1 and 53, respectively, wherein the assay further provides a second sbp member labeled with a ligand and immobilized on the capture zone by a receptor for the ligand coimmobilized on the capture zone. Katz discusses an assay having a biotinylated antibody attached to a capture zone via an avidin receptor. Applicants submit that because a *prima facie* case of obviousness based on Lou and Maggio has not been established with regard to base claims 1 and 53 (see ¶6), this rejection in view of Katz is similarly improper. Withdrawal of the rejection is respectfully requested.

¶10. Claims 12, 64, and 123 were rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Lou in view of Maggio as applied to claims 1, 4-6, 8, 11, 13, 14, 16-19, 21, 22, 53-58, 60, 63, 65-68, 70, 72-75, 77, 78, 80, and 120-122, and further in view of US 4,271,140 to Bunting. This rejection is respectfully traversed.

Claim 64 was previously canceled. Claim 12, and claim 123 as amended, are directed to assays having the same elements recited in claims 9 and 61, respectively, wherein the assay further provides a second sbp member labeled with a hapten and immobilized on the capture zone by a receptor for the hapten coimmobilized on the

capture zone. Bunting reports a double receptor, specific binding assay having a first receptor specific for a second receptor, the second receptor capable of binding a ligand.

Applicants submit that because a *prima facie* case of obviousness based on Lou and Maggio has not been established with regard to base claims 9 and 61 (see ¶9), this rejection in view of Bunting is similarly improper. Withdrawal of the rejection is respectfully requested.

¶11. Claims 10 and 62 were rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Lou in view of Maggio as applied to claims 1, 4-6, 8, 11, 13, 14, 16-19, 21, 22, 53-58, 60, 63, 65-68, 70, 72-75, 77, 78, 80, and 120-122, and further in view of US 4,943,522 to Eisinger et al. ["Eisinger"]. This rejection is respectfully traversed.

In brief, claims 10 and 62 are directed to assays having the same elements recited in claims 1 and 53, respectively, wherein the assay further provides a second sbp member that is an antibody against a complex formed between the analyte and the first sbp member. Eisinger discusses an assay having an antibody against a complex formed between an analyte and a binding member.

Applicants submit that because a *prima facie* case of obviousness based on Lou and Maggio has not been established with regard to original base claims 1 and 53 (see ¶6), this rejection in view of Eisinger is similarly improper. Withdrawal of the rejection is respectfully requested.

Rejections Under 35 U.S.C. §102

¶13. Claims 124 and 125 were rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Lou. This rejection is respectfully traversed.

Briefly, claim 124 is directed to an assay method, and claim 125 to an assay device, for quantifying analyte in a sample by providing, *inter alia*, a first sbp binding member that includes a visually detectable particulate or nonparticulate label, wherein the particulate label comprises dyed latex beads, erythrocytes, liposomes, dyes, sols, metallic colloids, or stained microorganisms.

Lou discusses an assay using colloidal selenium (a nonmetallic colloid) as a label. In contrast, claims 124 and 125 are drawn to exclude nonmetallic colloids. According to the MPEP 2131, to anticipate a claim, the reference must teach every element of the claim. Based on the above, Applicants submit that Lou fails to teach every element of claims 124 and 125. Withdrawal of this rejection is respectfully requested.

Allowable Subject Matter

¶14. The Examiner has indicated claims 15, 23, 69, and 79 are allowed.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**" Also attached, for the Examiner's convenient reference, are all the pending claims. This attachment is captioned "**Appendix of Pending Claims.**"

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claim 17 has been amended as follows.

17. (Amended) The method of claim 16, wherein the labeled first sbp member is an [a] antibody capable of binding the analyte.

Claim 77 has been amended as follows.

77. (Twice Amended) The device of claim 72, wherein the lateral flow matrix comprises a plurality of spatially separated capture zones.

Claim 121 has been amended as follows.

121. (Amended) A kit for determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), the kit comprising the device of claim 72 [74], a chart for correlating an observed accumulation of label at the one or more capture zones, to a concentration of analyte in a sample applied to the sample receiving zone, and instructions for using the device.

Claim 122 has been amended as follows.

122. (Amended) The device of claim 72 [53], wherein the first sbp member is a ligand and the second sbp member is a receptor complementary to the ligand.

Claim 123 has been amended as follows.

123. (Amended) The device of claim 61 [121] wherein the ligand is a hapten and the receptor is a complement to the hapten.

Claim 126 has been added as follows.

126. (New) A method of visually quantifying an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising:

providing a lateral flow matrix which defines a flow path and which comprises in series, a sample receiving zone, a labeling zone, and a single capture zone, wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte, and the capture zone comprises at least a second sbp

member uniformly immobilized in the capture zone, the second sbp member being complementary to the analyte;

contacting the sample with the sample receiving zone, whereby the sample flows along the flow path;

observing a pattern of label that accumulates at the capture zone whereby the pattern shows a distance traversed by the label along the single capture zone; and

correlating a pattern of label accumulated in the capture zone to the amount of analyte in the sample.

Claim 127 has been added as follows.

127. (New) A device for determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising a lateral flow matrix which defines a flow path and which comprises in series:

a sample receiving zone;

a labeling zone; and

a capture zone;

wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte, and the capture zone comprises at least a second sbp member uniformly immobilized in the capture zone, the second sbp member being complementary to the analyte.

Claim 128 has been added as follows.

128. (New) The method of claim 1, wherein the labeled first sbp member is an antibody capable of binding the analyte.

APPENDIX OF PENDING CLAIMS

1. (Amended) A method of visually quantifying an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising:

providing a lateral flow matrix which defines a flow path and which comprises in series, a sample receiving zone, a labeling zone, and one or more serially oriented capture zones, wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being complementary to the analyte;

contacting the sample with the sample receiving zone, whereby the sample flows along the flow path;

observing a pattern of label that accumulates at the one or more capture zones; and

correlating a pattern of label accumulated in the one or more capture zones to the amount of analyte in the sample.

4. The method of claim 1, wherein the labeled first sbp member is an antigand capable of binding the analyte.

5. The method of claim 1, wherein the first sbp member includes a visually detectable label.

6. The method of claim 5, wherein the visually detectable label comprises a visible particulate label.

7. The method of claim 1, wherein the second sbp member is attached to particles and the particles are immobilized in the capture zones.

8. (Amended) The method of claim 1, wherein the second sbp member is a ligand capable of binding the analyte.

9. The method of claim 1, wherein the second sbp member is labeled with a ligand and is immobilized on the capture zone by a receptor for the ligand coimmobilized on the capture zone.

10. (Amended) A method of visually quantifying an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising:

providing a lateral flow matrix which defines a flow path and which comprises in series, a sample receiving zone, a labeling zone, and one or more serially oriented capture zones, wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to or analogous to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being complementary to the analyte;

contacting the sample with the sample receiving zone, whereby the sample flows along the flow path;

observing a pattern of label that accumulates at the one or more capture zones; and

correlating a pattern of label accumulated in the one or more capture zones to the amount of analyte in the sample;

wherein the second sbp member is an antibody against a complex formed between the analyte and the first sbp member.

11. The method of claim 1, wherein the analyte is a polypeptidic molecule and the first and second sbp members are antibodies against different epitopes of the analyte.

12. The method of claim 9, wherein the ligand is a hapten and the receptor is a complement to the hapten.

13. The method of claim 1, wherein the lateral flow matrix comprises a plurality of spatially separated capture zones, and the step of observing a pattern of label that accumulates at the one or more capture zones comprises determining a number of capture zones at which label accumulates.

14. The method of claim 1, wherein the lateral flow matrix comprises a single capture zone having the second sbp member uniformly immobilized in the single capture zone and the step of observing a pattern of labeled first sbp member that accumulates at the one or more capture zones comprises observing a distance traversed by the label along the single capture zone.

15. (Amended) A method of visually quantifying an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising:

providing a lateral flow matrix which defines a flow path and which comprises in series, a sample receiving zone, a labeling zone, and one or more serially oriented capture zones, wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to or analogous to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being complementary to the analyte;

contacting the sample with the sample receiving zone, whereby the sample flows along the flow path;

observing a pattern of label that accumulates at the one or more capture zones; and

correlating a pattern of label accumulated in the one or more capture zones to the amount of analyte in the sample;

wherein the sample receiving zone comprises an amount of a third sbp member immobilized within the sample receiving zone and complementary to the analyte, the amount being sufficient to bind a threshold level of the analyte.

16. A method of determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising:

providing a lateral flow matrix which defines a flow path and which comprises in series, a sample receiving zone, a labeling zone, and one or more serially oriented capture zones, wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being analogous to the analyte;

contacting the sample with the sample receiving zone, whereby the sample flows along the flow path;

observing a pattern of labeled first sbp member that accumulates at the one or more capture zones; and

correlating a pattern of label accumulated in the one or more capture zones to the amount of analyte in the sample.

17. (Amended) The method of claim 16, wherein the labeled first sbp member is an antibody capable of binding the analyte.

18. The method of claim 16, wherein the labeled first sbp member includes a visually detectable label.

19. The method of claim 18, wherein the visually detectable label comprises a visible particulate label.

20. The method of claim 16, wherein the second sbp member is attached to particles and the particles are immobilized in the one or more capture zones.

21. The method of claim 18, wherein the lateral flow matrix comprises a plurality of capture zones, and the step of observing a pattern of label that accumulates at the one or more capture zones comprises determining a number of capture zones at which label accumulates.

22. The method of claim 18, wherein the lateral flow matrix comprises a single capture zone having the second sbp member uniformly immobilized in the single capture zone and the step of observing a pattern of labeled first sbp member that accumulates at the one or more capture zones comprises observing a distance traversed by the label along the single capture zone.

23. (Amended) A method of determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising:

providing a lateral flow matrix which defines a flow path and which comprises in series, a sample receiving zone, a labeling zone, and one or more serially oriented capture zones, wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being analogous to the analyte;

contacting the sample with the sample receiving zone, whereby the sample flows along the flow path;

observing a pattern of labeled first sbp member that accumulates at the one or more capture zones; and

correlating a pattern of label accumulated in the one or more capture zones to the amount of analyte in the sample;

wherein the labeled first sbp member includes a visually detectable label;
wherein the sample receiving zone comprises an amount of a third sbp member immobilized within the sample receiving zone and complementary to the analyte, the amount being sufficient to bind a threshold level of the analyte.

53. (Amended) A device for determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising a lateral flow matrix which defines a flow path and which comprises in series:

- a sample receiving zone;
- a labeling zone; and
- one or more serially oriented capture zones;

wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being complementary to the analyte.

56. (Amended) The device of claim 53, wherein the labeled first sbp member is an antibody capable of binding the analyte.

57. (Amended) The device of claim 53, wherein the first sbp member includes a visually detectable label.

58. (Amended) The device of claim 57, wherein the visually detectable label comprises a visible particulate label.

59. (Amended) The device of claim 53, wherein the second sbp member is attached to particles and the particles are immobilized in the capture zones.

60. (Amended) The device of claim 53, wherein the second sbp member is an antibody capable of binding the analyte.

61. (Amended) The device of claim 53, wherein the second sbp member is labeled with a ligand and is immobilized on the capture zone by a receptor for the ligand coimmobilized on the capture zone.

62. (Amended) A device for determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising a lateral flow matrix which defines a flow path and which comprises in series:

a sample receiving zone;

a labeling zone; and

one or more serially oriented capture zones;

wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to or analogous to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being complementary to the analyte;

wherein the second sbp member is an antibody against a complex formed between the analyte and the first sbp member.

63. (Amended) The device of claim 53, wherein the analyte is a polyepitopic molecule and the first and second sbp members are antibodies against different epitopes of the analyte.

65. (Amended) The device of claim 53, wherein the analyte is human IgE.

66. (Amended) The device of claim 65, wherein the first sbp member is goat anti-human IgE and the second sbp member is mouse monoclonal anti-human IgE.

67. (Amended) The device of claim 53, wherein the lateral flow matrix comprises a plurality of spatially separated capture zones.

68. (Amended) The device of claim 53, wherein the lateral flow matrix comprises a single capture zone having the second sbp member uniformly immobilized in the single capture zone.

69. (Amended) A device for determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising a lateral flow matrix which defines a flow path and which comprises in series:

a sample receiving zone;

a labeling zone; and

one or more serially oriented capture zones;

wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to or analogous to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being complementary to the analyte;

wherein the sample receiving zone comprises an amount of a third sbp member immobilized within the sample receiving zone and complementary to the analyte, the amount being sufficient to bind a threshold level of the analyte.

70. (Amended) The device of claim 53, wherein the device comprises a plurality of discrete lateral flow matrices.

71. (Amended) The device of claim 70, wherein the plurality of discrete lateral flow matrices have a common sample receiving zone, whereby a sample deposited in the sample receiving zone flows along each of the lateral flow matrices.

72. A device for determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), the device comprising a lateral flow matrix which defines a flow path and which comprises in series:

- a sample receiving zone;
- a labeling zone; and
- one or more serially oriented capture zones;

wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being analogous to the analyte.

73. (Amended) The device of claim 72, wherein the labeled first sbp member is an antibody capable of binding the analyte.

74. (Amended) The device of claim 72, wherein the labeled first sbp member includes a visually detectable label.

75. (Amended) The device of claim 74, wherein the visually detectable label comprises a visible particulate label.

76. (Amended) The device of claim 72, wherein the second sbp member is attached to particles and the particles are immobilized in the one or more capture zones.

77. (Twice Amended) The device of claim 72, wherein the lateral flow matrix comprises a plurality of spatially separated capture zones.

78. (Amended) The device of claim 72, wherein the lateral flow matrix comprises a single capture zone having the second sbp member uniformly immobilized in the single capture zone.

79. (Amended) A device for determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), the device comprising a lateral flow matrix which defines a flow path and which comprises in series:

- a sample receiving zone;
- a labeling zone; and
- one or more serially oriented capture zones;

wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being analogous to the analyte;

wherein the sample receiving zone comprises an amount of a third sbp member immobilized within the sample receiving zone and complementary to the analyte, the amount being sufficient to bind a threshold level of the analyte.

80. (Amended) The device of claim 72, wherein the device comprises a plurality of discrete lateral flow matrices.

81. The device of claim 80, wherein the plurality of discrete lateral flow matrices have a common sample receiving zone, whereby a sample deposited in the sample receiving zone flows along each of the lateral flow matrices.

120. (Amended) A kit for determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), the kit comprising the device of claim 53, a chart for correlating an observed accumulation of label at the one or more capture zones, to a concentration of analyte in a sample applied to the sample receiving zone, and instructions for using the device.

121. (Amended) A kit for determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), the kit comprising the device of claim 72, a chart for correlating an observed accumulation of label at the one or more capture zones, to a concentration of analyte in a sample applied to the sample receiving zone, and instructions for using the device.

122. (Amended) The device of claim 72, wherein the first sbp member is a ligand and the second sbp member is a receptor complementary to the ligand.

123. (Amended) The device of claim 61 wherein the ligand is a hapten and the receptor is a complement to the hapten.

124. A method of visually quantifying an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising:

providing a lateral flow matrix which defines a flow path and which comprises in series, a sample receiving zone, a labeling zone, and one or more serially oriented capture zones, wherein the labeling zone comprises a diffusively bound labeled first sbp member that is analogous to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being complementary to the analyte;

contacting the sample with the sample receiving zone, whereby the sample flows along the flow path;

observing a pattern of label that accumulates at the one or more capture zones; and

correlating a pattern of label accumulated in the one or more capture zones to the amount of analyte in the sample;

wherein said first sbp member includes a visually detectable particulate or nonparticulate label, said particulate label comprising dyed latex beads, erythrocytes, liposomes, dyes sols, metallic colloids, or stained microorganisms.

125. A device for determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising a lateral flow matrix which defines a flow path and which comprises in series:

- a sample receiving zone;
- a labeling zone; and
- one or more serially oriented capture zones;

wherein the labeling zone comprises a diffusively bound labeled first sbp member that is analogous to the analyte, and each of the one or more capture zones comprises at least a second sbp member immobilized in the capture zone, the second sbp member being complementary to the analyte;

wherein said first sbp member includes a visually detectable particulate or nonparticulate label, said particulate label comprising dyed latex beads, erythrocytes, liposomes, dyes sols, metallic colloids, or stained microorganisms.

126. (New) A method of visually quantifying an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising:

providing a lateral flow matrix which defines a flow path and which comprises in series, a sample receiving zone, a labeling zone, and a single capture zone, wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte, and the capture zone comprises at least a second sbp member uniformly immobilized in the capture zone, the second sbp member being complementary to the analyte;

contacting the sample with the sample receiving zone, whereby the sample flows along the flow path;

observing a pattern of label that accumulates at the capture zone whereby the pattern shows a distance traversed by the label along the single capture zone; and

correlating a pattern of label accumulated in the capture zone to the amount of analyte in the sample.

127. (New) A device for determining an amount of an analyte in a sample, wherein the analyte is a member of a specific binding pair (sbp member), comprising a lateral flow matrix which defines a flow path and which comprises in series:

a sample receiving zone;

a labeling zone; and

a capture zone;

wherein the labeling zone comprises a diffusively bound labeled first sbp member that is complementary to the analyte, and the capture zone comprises at least a second sbp member uniformly immobilized in the capture zone, the second sbp member being complementary to the analyte.

128. (New) The method of claim 1, wherein the labeled first sbp member is an antibody capable of binding the analyte.